

Claims 1 through 3 and 8 through 11 are pending, Claims 4-7 having been canceled as non-elected claims without prejudice.

Why This Amendment Should Be Entered After Final Rejection

This amendment should be entered although after Final Rejection, because it provides a further explanation of one important aspect of the invention, not yet understood by the Examiner; and this further explanation puts the case as a whole in better condition for Appeal.

One of the important limitations of the claimed invention is that the hydroxyethyl starch has a "ratio of the substitution of C2 to the substitution of C6 of the anhydroglucose units ...[being] 8-20 ...". As defined in the specification at page 3, paragraph 1, this ratio means that the hydroxyethyl starches have a high ratio of substitution at C2 versus at C6 of the anhydroglucose unit, thus there is predominately C2 substitution (page 7, paragraph 1, page 6, paragraph 2). Or, to paraphrase the claim language, "the ratio of the substitution of C2 to the substitution of C6" in these substituted anhydroglucose units "is 8-20". "The ratio "8-20" means hydroxyethyl starch having from 8 anhydroglucose units substituted at C2 per 1 anhydrous unit substituted at C6 up to 20 anhydroglucose units substituted at C2 per anhydroglucose unit substituted at C6."

Despite Applicants' detailed explanation of the meaning of this ratio in their June 22, 1992 Amendment (page 4, paragraph 3 - page 5, paragraph 1), the Examiner continues to misunderstand the meaning of this ratio. More importantly, due to this misunderstanding, the Examiner is maintaining the obviousness rejection of Applicants' claim.

Therefore, Applicants seek herein to explain even more thoroughly how the C2: C6 ratio of Claim 1 differs from that of the cited art: and why the references cited by the Examiner cannot render Claim 1 obvious. It is submitted that entry of the instant

amendment will, by virtue of the further explanation of the C2:C6 ratio in Claim 1, present the rejected claims in better form for consideration on appeal. It is further noted that the arguments presented herein were not earlier presented because Applicants' reasoning in the prior amendment was believed fully to overcome the obviousness rejection.

In light of the above, Applicants submit the instant amendment merits being entered despite being submitted after Final Rejection.

#### Priority Document

Regarding the Examiner's acknowledgement of the priority claimed, Applicants submit herewith the priority document upon which the priority claim is based: DE P 39 19729.8.

#### Section 103 Rejection

##### (a) The cited art does not teach the "8-20" ratio range of Claim 1.

In maintaining the obviousness rejection from the preceding Official Action, the Examiner again concedes that primary reference Nitsch, et al. fails to teach "the specific molar substitution and C<sub>2</sub> to C<sub>6</sub> ratio" (page 4, line 6, August 17, 1992 Official Action). The Examiner asserts that this shortcoming in the primary reference is cured by a teaching in Morishita.

As Applicants explained at some length in their June 24, 1992 Amendment (page 4, paragraph 3 - page 5, paragraph 1), Morishita teaches an HES having a C2:C6 ratio far different from that of Claim 1, i.e. from 0.5 to 2.0. Despite this detailed explanation and the Examiner's assurance that Applicants arguments "have been fully considered," the Examiner still considers that the C2:C6 ratio of Morishita is equivalent to a ratio of 5 to 20, which overlaps that of amended Claim 1.

However, by its own terms, Morishita teaches that its 0.5-2.0 ration is not

equivalent to a ratio of 5 to 20. Morishita explains the ratio as follows: one of its objects is to "provide a hydroxyethylstarch having more substituted hydroxymethyl groups on carbon atom 6 than on carbon atom 2 of the glucose ring" (page 1, line 13-15). In other words, the Morishita ratio of 0.5 to 2.0 corresponds to hydroxyethylstarches having "more hydroxyethyl groups substituted in the primary alcohol on the carbon atom 6 than on the carbon atom 2 for example, starch with a 2-O-HEG ... of the glucose ring" (page 2, lines 1-7).

Given these very clear references in Morishita to the glucose ring, it is clear the 0.5-2.0 ratio means from 0.5 substitutions at C2: 1 substitution at C6 up to 2.0 substitutions at C2:1 substitution at C6 of the glucose ring. This latter ratio is incompatible with the one previously quoted above and is thus confusing. When this is appreciated, it becomes clear that the Examiner's shifting the Morishita ratio of 0.5 to 2.0 up to 5-20 is completely impermissible.

Table I at page 4 of Morishita discloses a C2 to C6 ratio of 10.8 through 0.5. However, from the claims and from the text of the specification, it is clear Morishita actually teaches away from the ratio range of Claim 1, i.e. it favors far more substitution at C6 than at C2 (page 1, lines 6-9; page 1, lines 13-15; page 2, lines 1-8; and page 3, lines 1-7). Thus, it is clear that the "found" ratios of 0.5 and 0.8 are preferred, i.e., more on C6 and 2.0, i.e., slightly more on C2 is tolerated. Thus, more than 2.0 on C2 is disfavored by Morishita.

Clearly, Applicants' finding of "8-20" on C2, while it overlaps the disclosure of Table I, cannot be suggested by Morishita since this reference indicates this range to be disfavored.

The Examiner obtains the ratio range 5 through 20 by multiplying the expression 0.5 through 2.0 by 10. However, in doing so he overlooks the fact that the expression "0.5 through 2.0", denotes the ratio range from 0.5:1 through 2.0:1.

In such a ratio range, one is concerned with a relationship and thus, if some values are multiplied by 10, all values must be multiplied by 10. This means that if the multiplication utilized by the Examiner is correctly applied, the original ratio range of 0.5:1 through 2.0:1 becomes 5:10 through 20:10. Thus, the Examiner's derived range neither equals that 0.5:1 to 2.0:1 nor overlaps the 8:1 to 20:1 range of Applicants' Claim 1.

Applicants submit that by altering the Morishita ratio of 0.5-2.0 to 5-20, the Examiner has overlooked the actual teachings of the reference in favor of a hindsight interpretation. "The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification." In re Fritch, \_\_ USPQ2d \_\_ (August 11, 1992, Vol. 44 BNA Patent, Trademark & Copyright Journal, p. 400). Furthermore, it appears the Examiner has disregarded an important difference between the claimed invention and the cited prior art and so, failed to apply the test mandated by the U. S. Supreme Court in Graham v. John Deere 383 US 1 (1966).

(b) Staley is not combinable with Nitsch et al.

Staley is not directed to Hydroxyethyl starch but rather to hydroxyalkyl amylose. The reference is not directed to formation of plasma expanders, but rather to formation of hydroxyalkyl amylose for the formation of films. It is immediately apparent that such film products will have properties other than those suitable for plasma expanders. Thus, one skilled in the art would not adopt any teaching of Staley regarding the characteristics which are desirable for HES plasma expanders.

(c) The obviousness analysis has overlooked surprising properties of the claimed HES compounds.

The advantageous properties inherent in the claimed compositions are part of the claimed subject matter, despite the Examiner's dismissal of these properties, set forth in the Declaration under 37 CFR 1.132 filed December 22, 1991. Because these

properties constitute part of the subject matter of the invention, they must be considered in evaluating the differences over the prior art. Insofar as the Examiner has not considered the superior elimination time, the obviousness analysis is incomplete and ought not to stand.

(d) Even if combined, the cited references fail to lead to Claim 8.

While certain steps of Nitsch et al. may resemble those of Claim 8, various conditions of the process are different. In Nitsch et al., acid hydrolysis is not used alone. Instead, at least a partial enzymatic hydrolysis is employed (col. 2, first and second paragraphs). Enzymatic hydrolysis of the starch, used alone or with acid hydrolysis, produces a branching pattern in the starch product different from that if acid hydro-lysis alone is used. Acid hydrolysis is a statistically running process; by contrast, enzymatic hydrolysis cleaves only alpha 1,4 bonds of starch.

Thus it is clear that Nitsch et al. must produce significantly different starch than the process of Claim 8. Even if the products of this reference and Claim 8 have identical molecular weight and mass spectra, the differing branching patterns clearly indicates the products are not equivalent. Further differences are found in the differing DS, C2:C6 ratios, and the etherization procedures (as pointed out in Applicants' December 16, 1991 Amendment, page 4, paragraphs 2 and 3; and June 24, 1992 Amendment page 6, paragraph 1). Given these numerous differences between the products of Nitsch et al. and Claim 8, it is clear these processes themselves differ greatly.

For the above reasons, reconsideration and withdrawal of the obviousness rejection are requested.

Applicants acknowledge the Examiner's view that arguments in the preceding amendment were phrased in language indicative of an anticipation rejection. Applicants vigorously traverse this assertion and any implication that the prior

amendment was not fully responsive. In this regard the Examiner's attention is drawn to page 4, paragraph 2 and page 6, paragraphs 3 and 4 of the June 24, 1992 amendment.

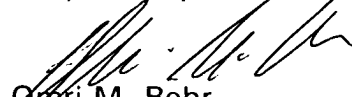
Restriction Requirement

Applicants acknowledge the Examiner's comments regarding the Restriction Requirement. By canceling Claims 4 through 7 without prejudice, Applicants believe they have fully responded to all matters connected with the Restriction Requirement.

Finally Applicants acknowledge the Examiner's remarks on the Declaration under 37 CFR 1.132 filed December 20, 1991. Applicants comments at page 5, paragraphs 1 and 2 of their December 16, 1991 Amendment explaining the relevance of the Declaration test results are reiterated. However, Applicants submit no further declaratory evidence need be submitted, because the Examiner has failed to establish prima facie obviousness.

In view of the above, favorable action with respect to all the claims and prompt advancement to allowance thereof are requested.

Respectfully submitted,

  
OMRI M. Behr  
Regis. No. 22,940

Telephone (908) 494-5240

OMB/MJM/cg

c:\wp51\doc\lud36u2.amd  
b:lud36c2.amd

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231.

by 16 Oct 92

OMRI M. BEHR

Attorney for Applicant, Reg. No. 22,940

Signed: 

Date of Signing: 16 Oct 92